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## REMARKS

Claims 11-22 have been canceled as directed at non-elected subject matter. Applicants reserve the right to re-introduce claims 11-22 in one or more subsequent divisional applications without prejudice. Claim 1 has also been canceled and claim 10 has been amended to recast it into an independent form which more distinctly claims the elements which comprise the invention. Claims 2-9 all ultimately dependent on amended claim 10.

**Claim 1 is rejected under 35 U.S.C.103(a) as being unpatentable over US 3930005.**

Claim 1 has been canceled. Claim 10 as currently amended affords a process for which allows the introduction of a desired substituent at the 2-, 6-, 8- and 9-positions can be from a common starting material, a 4,6-dihalo-5-nitro-2-thioether pyrimidine. The flexibility to introduce structural diversity from a common starting material is highly advantageous in compound library synthesis. In contrast, the process disclosed in US 3930005 requires a unique starting material in which the 2- and 9-substituents are fixed at the outset of the synthesis requiring a unique starting material for each combination of substituents at to 2- and 9-positions.

**Claim 9 is rejected under 35 U.S.C. 35 103(a) as being unpatentable over US 3930005 as applied to claim 1 above, further in view of DiLucrezia.**

DiLucrezia does not teach a process that allows functionalization of the 2-position of the purine ring. The process disclosed by DiLucrezia only contains an amino group at the 6-position and only variation of the 8- and 9-positions is disclosed. Although DiLucrezia and US 3930005 both teach methods to form the imidazole ring with various substitution at the 8-position of the newly formed purine, neither teaches all the elements of the invention as currently claimed, *i.e.* a process allowing selective functionalization of all four positions of the purine ring.

In order to establish *prima facie* obviousness, three basic criteria must be met. First, the prior art must provide one of ordinary skill in the art with a suggestion or motivation to modify or combine the teachings of the references relied upon by the PTO to arrive at the claimed invention. The suggestion or motivation to combine generally arises in the references, but may also be inferred from the nature of the problem or the knowledge of those of ordinary skill in the art. *WMS Gaming Inc. v. International Game Technology*, 51 USPQ2d 1385, 1397 (Fed. Cir. 1999).

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The mere fact that references could be modified or combined does not render the resultant modification or combination obvious unless the prior art also suggests the desirability of the modification or combination. *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990); MPEP § 2143.01. Second, the prior art must provide one of ordinary skill in the art with a reasonable expectation of success. Thus, in light of the teachings of the prior art, the skilled artisan must have a reasonable expectation that the modification or combination suggested by the Examiner would succeed. *In re Dow*, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988). Third, either alone or in combination, the prior art must teach or suggest each and every limitation of the rejected claims. *In re Gartside*, 53 USPQ2d 1769 (Fed. Cir. 2000). The teaching or suggestion to make the claimed invention, as well as the reasonable expectation of success, must come from the prior art and not Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). If any one of these criteria are not met, *prima facie* obviousness is not established, and Applicants are not required to show new or unanticipated results. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985).

There is no suggestion in the references cited which would motivate the skilled artisan to combine the reactions as described herein to produce a process to prepare fully substituted purines. Withdrawal of the rejection under 35 U.S.C. §103(a) is requested.

Claims 1-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which the applicant regards as his invention.

1. The terms "thioalkyl" and "thioaryl" are asserted to be non-standard nomenclature.

The amendment to claim 10 now incorporates the terms "alkylthio" and "arylthio". The specification also has been amended on page 11, lines 9-12 to correct the usage. The definitions on page 11 clearly define the meaning of the terms and the amendments do not comprise any new matter.

2. The nature of the heterocycle formed by  $\text{NR}^8\text{R}^9$  is asserted to be unclear.

The definition of a "heterocycle" from page 9, line 23 to page 10, line 2 of the specification has now been explicitly incorporated into the definition of  $\text{R}^5$  which is now

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in claim 10. The incorporated definition has been adapted to the particular situation requiring that at least one heteroatom is nitrogen (i.e.,  $\text{NR}^8\text{R}^9$ ) and if the second heteroatom is nitrogen it is either unsubstituted ( $\text{R}^{10}$  is hydrogen) or a tertiary amine ( $\text{R}^{10}$  is alkyl). The definition on page 10 allows optional alkyl substitution. No new matter is believed to be incorporated by this amendment to the claims.

3. Claim 5 is not worded correctly. A step cannot comprise a thing.

Claim 5 has been amended as suggested in the Office Action.

4. Claims 6 and 7 are unclear because the terms "substantially free of" and "substantially all of" are indefinite.

The specification contains a definition of the term "substantially free of" of on page 11, lines 5-8. The definition identifies ranges of less than 10, 5, 1 and 0.1 mole percent. Claims 6 and 7 have been amended to incorporate the definitions "contains less than 10 mole percent" and "more than 90 mole percent" respectively.

5. The term "acyl anhydride" is asserted to be unclear.

Claim 9 has been amended to change "acyl anhydride" to --carboxylic acid-- anhydride.

6. The term "metal complex" in claim 10 is asserted to be indefinite.

A non-limiting list of reagents used to displace the alkylsulfonyl group can be found on page 18, line 24 to page 19 line 6 of the specification. It is well known that none of the metals represented by M form simple ion pair salts and all are dimeric or multimeric aggregates including anionic ligands and/or solvents of varying levels of complexity. Thus it is not possible or conventional to describe the precise species in solution. One skilled in the art will immediately appreciate how the  $\text{R}^5$  moieties can be converted into nucleophiles capable of displacing a leaving group. In order to expedite the examination claim 10 has been amended to recite specific metals which could be used in the present case. A discussion of reagents to displace the leaving group at the 2-position can be found on page 18 line 24 to page 19, line 6. The discussion refers generically to

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alkoxides and aryloxides and these are routinely converted to sodium and potassium salts to carry out displacements (e.g., the Williamson ether synthesis). Enolates and malonates are routinely converted to nucleophiles by forming the lithium, sodium or potassium (i.e. and alkali metal) salt. Thus no new matter is believed to be introduced by the amendment.

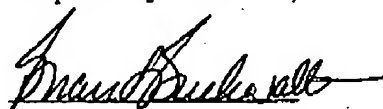
#### SUPPLEMENTARY IDS

A supplementary Form 1449 is included which cites R. C. Thummel *et al.* EP 0 084 758. No English language version was available. Applicants note that claim 5 (English translation on page 7, line 53 to page 8, line 15) which teaches the displacement of an alkylsulfone with an amine. Applicants further note that on page 2, line 51 the disclosure suggests to [t]he group -X-R<sub>4</sub> is particularly C<sub>1-4</sub> thioalkyl and C<sub>1-3</sub> alkoxy.

#### CONCLUSIONS

Applicants believe that the claims as amended are in condition for allowance. The sequence of the claims should be reordered as follows: 10-2-3-4-5-6-7-8-9. Examiner is authorized to deduct the fee under 37 CFR 1.17(a)(1) for a one month extension and the fee under 37 CFR 1.17(p) for submission of an IDS from our deposit account 18-1700. If the Examiner believes a telephone conference will expedite the prosecution of this application, the Examiner is invited to contact the undersigned at the number indicated below.

Respectfully submitted,



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